

**PROCEDURE FOR PRIORITIZING CHEMICALS
FOR CONSIDERATION UNDER PROPOSITION 65
BY THE "STATE'S QUALIFIED EXPERTS"**

UPDATE – May, 2004 DRAFT

Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

BACKGROUND

The Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65, California Health and Safety Code section 25249.5 *et seq.*) requires the Governor to publish a list of chemicals known to cause cancer or reproductive toxicity. One of the mechanisms by which a chemical is placed on this list is a finding by the “state’s qualified experts” that a chemical “has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity.” (Health and Safety Code section 25249.8(b)) As the lead agency for the implementation of Proposition 65, the Office of Environmental Health Hazard Assessment (OEHHA) has formed the Science Advisory Board (SAB), which includes two committees of independent scientists and health professionals that serve as the state’s qualified experts. These committees are the Carcinogen Identification Committee (CIC) and the Developmental and Reproductive Toxicant Identification Committee (DART IC).

This document describes a process used by OEHHA staff to identify chemicals for evaluation by the CIC and DART IC. The process is designed to ensure that the efforts of these committees are focused on chemicals that may pose significant hazards to Californians. As with

the previous process (OEHHA, 1997), this process includes opportunities for public input at multiple points.

The CIC at its December 2002 meeting asked OEHHA to develop this process as an alternative to the prioritization process currently in use. The CIC specifically asked for an alternative process that could better take into account the level of exposure and population potentially affected by various chemicals being reviewed by OEHHA, as well as the degree and extent of potential harm posed by the chemicals. The CIC also asked OEHHA to address the deficiencies in the current process and the costs of the alternative process. Deficiencies noted in the current process include the significant length of time needed to conduct prioritizations, the considerable staff resources expended, and the public health importance of chemicals reaching the committees.

The prioritization process also affects the work of the DART IC and, after consultation with the Director of OEHHA, the Chair of the DART IC asked that the DART IC be involved in developing an alternative prioritization process. The Prioritization Subcommittee, formed as a subcommittee of the DART IC and CIC, is advising OEHHA in this effort. The process proposed in this document is the outcome of the subcommittee's activities. When finalized, this prioritization process will replace the existing one described in OEHHA's 1997 document, "Procedure for Prioritizing Candidate Chemicals for Consideration under Proposition 65 by the 'State's Qualified Experts'."

The goal of this process is to efficiently prioritize chemicals for development of hazard identification materials and subsequent CIC and DART IC review.

The prioritization process is based on a preliminary appraisal of the evidence of hazard for the purpose of identifying chemicals for potential committee review. The cost in staff resources and time required to conduct the proposed process are not expected to exceed those of the previous process. Complicated scientific issues concerning chemicals under consideration are not addressed in the prioritization process but may be addressed, as needed, in the development of hazard identification materials. For example, the relevance of a particular tumor type to humans, interspecies differences in toxicity or pharmacokinetics, or establishment of the most appropriate exposure metric in an epidemiology study will be examined in detail in hazard identification materials prepared for CIC or DART IC consideration, rather than during the prioritization process.

The prioritization process described here is the primary method by which a chemical can reach the CIC or DART IC for consideration. In addition, a chemical may be referred to the CIC or DART IC when it is found not to meet the criteria for authoritative bodies listing subsequent to the issuance by OEHHA of a Notice of Intent to List (Title 22, Cal. Code of Regs. §12306). The Director of OEHHA at his or her discretion may decide to abbreviate or modify the process when necessary. In all such cases, OEHHA will post public notices in the *California Regulatory Notice Register* and on its Web site. Finally, OEHHA proposes, as appropriate, to bring to the relevant committee chemicals listed in Title 22, Cal. Code of Regs. § 14000 (Health and Safety Code section 25249.8(c)) because they are required by State or Federal law to be tested for

carcinogenicity or reproductive toxicity, once the required testing has been completed. If the resulting tests provide adequate data showing that a chemical causes cancer or reproductive toxicity, the chemical may be brought to the relevant committee for consideration.

PRIORITIZATION PROCESS

The following lays out the steps that OEHHA proposes to use in selecting chemicals for consideration by the CIC and DART IC. This prioritization process will be conducted on a periodic basis, with no set interval, and it will be rerun as needed. Figure 1 is a flow chart of the prioritization process.

- ***Tracking database.*** OEHHA maintains tracking databases of chemicals that have come to OEHHA's attention for DART or carcinogenicity evaluation. A chemical may be grouped with other, similar chemicals at various stages in the prioritization process. For example, groupings may result from similarity in chemical structure, mechanistic considerations, or the production of the same or similar proximate active dissociation products or metabolites. Examples of chemical groupings that have been reviewed by the CIC or DART IC are: aflatoxins and polychlorinated biphenyls (similarity of chemical structure and mechanism), inorganic oxides of arsenic (same active dissociation product), alcoholic beverages (same set of proximate carcinogens), and radionuclides (similarity of mechanism and active agent).
- ***Candidate Chemicals.*** Chemicals entered into a tracking database maintained by OEHHA would be investigated for the existence of relevant toxicity data and the

potential for human exposure. Those that exhibit data suggesting they cause reproductive toxicity or cancer and have exposure potential in California would become candidate chemicals.

The toxicity evaluation at this stage would involve the identification of one or more studies suggesting cancer or reproductive effects in animals or humans. The evaluation of exposure potential in California would be qualitative and would not involve prediction of levels of exposure. Production, use, or monitoring data could provide qualitative evidence of exposure potential. In the absence of information specific to California, data on production, use and environmental levels at the national level would generally be assumed to reflect the situation in California.

- ***Proposed Chemicals for Committee Consideration.*** Candidate chemicals would be screened using a focused literature review as recommended by the CIC/DART IC Prioritization Subcommittee. The Prioritization Subcommittee recommended that initially all candidate chemicals should undergo an epidemiology data screen. This would involve the identification of those chemicals with epidemiological evidence suggesting they cause cancer or reproductive toxicity. The type of literature review screen would change over time, based on Subcommittee recommendations. The literature review could be based upon the original research articles, or literature compilations or reviews. A chemical that does not pass the screen would remain as a candidate chemical at this time but would be reevaluated using future screens. After chemicals have passed a screen and considered for HID development, the process would

start over using another screen (e.g., for carcinogens, positive animal evidence) as recommended by the Prioritization Subcommittee.

Chemicals selected by the screen would undergo preliminary toxicological evaluation to determine whether they should be proposed for committee consideration. At this stage the overall evidence of carcinogenicity or reproductive toxicity of the chemical would be considered, including epidemiologic, animal bioassay, and other relevant information, as appropriate. This preliminary overall evaluation could be based on original research articles, or literature compilations or reviews.

Adverse developmental effects that co-occur with maternal toxicity, and reproductive effects that co-occur with systemic toxicity would be considered evidence of reproductive toxicity unless these toxicities are so severe as to preclude interpretation of the study (U.S. EPA, 1991, 1996). In animal data evaluations, effects would be assumed to be relevant to humans, unless OEHHA determines there is compelling evidence to the contrary.

Public comment and submission of chemical list to the relevant committee. The list of chemicals proposed by OEHHA for CIC or DART IC consideration for listing would be released to the public for comment, along with the rationale for the selection. A notice identifying OEHHA's list of chemicals proposed for committee consideration would be published in the *California Regulatory Notice Register* and posted on OEHHA's Web site. This would begin a 60-day public comment period. OEHHA would then compile

public comments and send them to the relevant committee, along with the list of chemicals proposed for review and related rationale. Appraisals of the evidence to support a proposal for review by the CIC or DART IC would be qualitative. This initial evaluation by its nature would be abbreviated and would not be as intensive or thorough as a hazard evaluation. It would simply be a preliminary appraisal for the purpose of identifying chemicals for further evaluation and potential committee review. The in-depth review of toxicological data would occur at a later stage, when hazard identification materials are developed.

- ***Committee Consultation on Chemicals for Review.*** During the CIC and DART IC meetings, OEHHA would receive consultation from the committees on the list of chemicals proposed for committee consideration. That is, the committee would advise OEHHA on the chemicals that should undergo the development of hazard identification materials, committee review and listing decision. The CIC would advise on chemicals for carcinogenicity hazard identification, and the DART IC would advise on chemicals for reproductive toxicity hazard identification. The committees could also suggest other chemicals worthy of review. At the committee meeting, the public would be given the opportunity to comment on chemicals being proposed for review. The committees could vote on recommendations, or could provide less formal advice.
- ***OEHHA Selection of Chemicals for Hazard Identification Materials.*** OEHHA will select the chemicals for the development of hazard identification materials.

The prioritization process ends with the selection of chemicals by OEHHA for hazard identification materials. The next steps in the process, described below, are those of hazard identification for the purposes of Proposition 65.

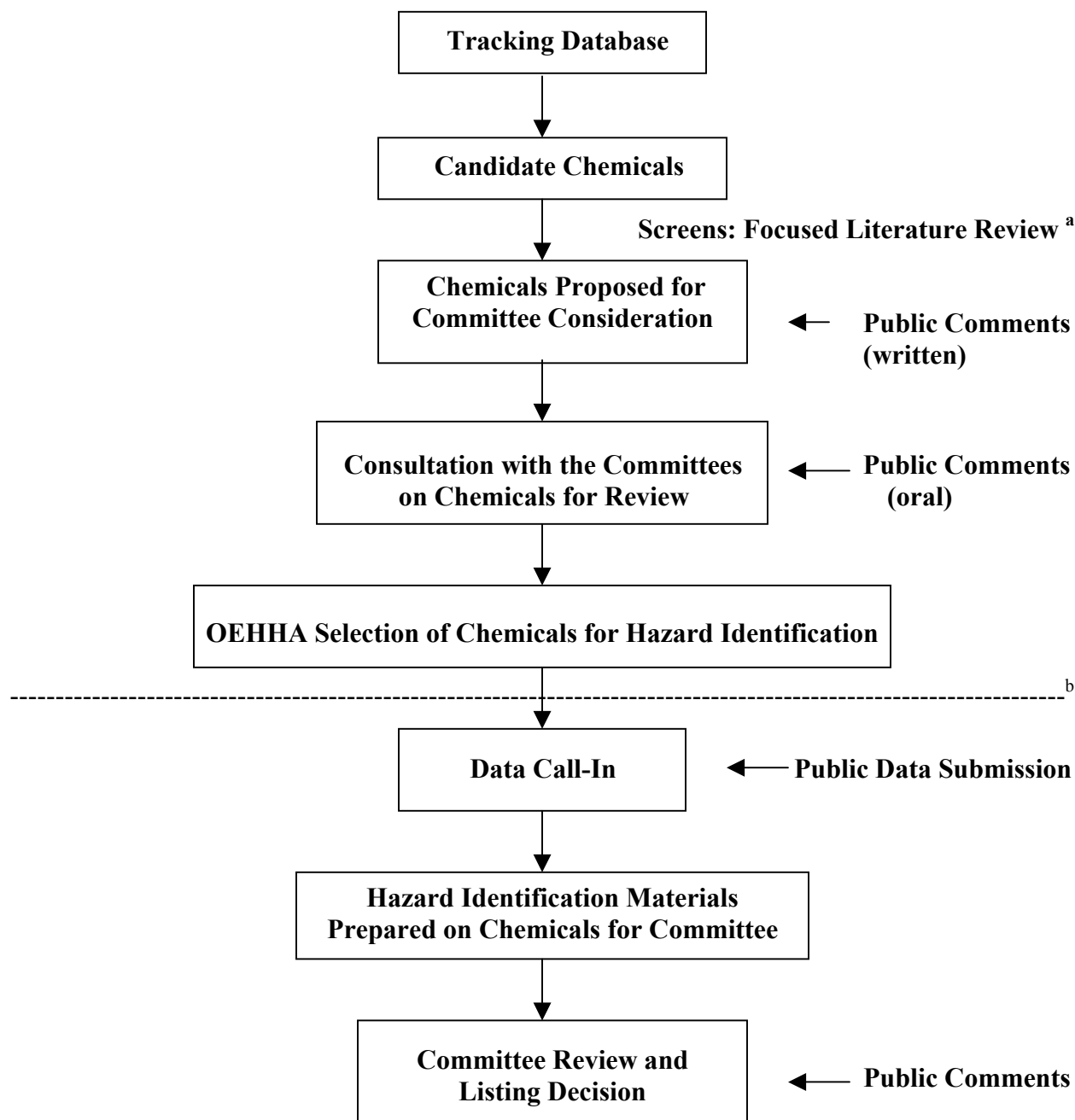
- ***Data Call-In.*** OEHHA solicits information on the evidence for carcinogenicity or reproductive toxicity on chemicals selected for review. A “data call-in” notice published in the *California Regulatory Notice Register* and posted on OEHHA’s Web site requests information relevant to the preparation of hazard identification materials on the chemicals selected for review.
- ***Hazard Identification Materials on Chemicals for Committee Review.*** Hazard identification materials are prepared for CIC or DART IC consideration and released to the public for comment. OEHHA decides the order in which these materials are prepared based on considerations such as committee advice and staff resources. The public is invited to comment on the hazard identification materials during a 60-day public comment period. Approximately two weeks before the public meeting, the public comments are collated and sent to the relevant committee for consideration along with the hazard identification materials developed by OEHHA.
- ***Committee Review and Decision on Listing.*** The CIC or DART IC holds a public meeting to deliberate on whether the chemical has been clearly shown to cause cancer or reproductive toxicity. The hazard identification materials and the public comments received during the 60-day comment period are considered at the meeting. The public

has a further opportunity to comment at the meeting. At the conclusion of the deliberations, the committee generally renders an opinion as to the developmental or reproductive toxicity or carcinogenicity of a chemical, as appropriate. In considering groups of chemicals, the committee may make findings for individual members of the group, or the group as a whole (e.g. arsenic [inorganic oxides]).

LEGAL CONSIDERATIONS

The prioritization process is, and has always been, intended to be used by OEHHA as a general process for prioritization of chemicals for committee consideration. The Director may abbreviate or otherwise modify the process when necessary. The process does not now, nor has it ever had the force of a regulation. Based upon Health and Safety Code section 25249.8(e), the development and implementation of the process is not subject to the provisions of the Administrative Procedure Act.

Figure 1. Prioritization Process



^a First screen based on epidemiological evidence; subsequent screens based on committee recommendations.

^b Dotted line indicates where the prioritization process ends and hazard identification process begins.

REFERENCES

Office of Environmental Health Hazard Assessment (OEHHA, 1997). Procedure for Prioritizing Candidate Chemicals for Consideration under Proposition 65 by the “State’s Qualified Experts.”

OEHHA, Reproductive and Cancer Hazard Assessment Section, Sacramento.

U.S. Environmental Protection Agency (U.S. EPA, 1991). Guidelines for Developmental Toxicity Risk Assessment. *Federal Register* 56(234): 63798-63826.

U.S. Environmental Protection Agency (U.S. EPA, 1996). Guidelines for Reproductive Toxicity Risk Assessment. *Federal Register* 61(212): 56274-56322.